Fructose in Diabetes Mellitus

SIR,—In your annotation (*Journal*, February 27, p. 510) concerning the intravenous administration of fructose, you state that "fructose may prove to be a more useful sugar in conditions where glucose has a time-honoured place—for example, in the treatment of hypoglycaemia." It is the purpose of this letter to draw attention to another hexose sugar that merits study—namely, mannose.

Mannose is slowly absorbed from the gastro-intestinal tract, but if given intravenously there is every evidence that it is well utilized and capable of forming glycogen in the liver and muscles. As long ago as 1924 mannose was shown to be as effective as glucose, and much better than fructose, in preventing the symptoms of insulin hypoglycaemia in experimental animals.[1] Moreover, like fructose but not like glucose, mannose disappears rapidly from the blood stream in the absence of insulin.[2] It is as effective as either glucose or fructose in supporting the respiration of isolated brain tissue.[3] Mannose is as good as glucose, and much better than fructose, in supporting the metabolic turnover of pentosenucleic acid[4] and phospholipid[5] in respiring brain slices. Mannose, like glucose and unlike fructose, can maintain the life of an animal after the removal of the liver[6] and, again like glucose and unlike fructose, can restore to normal the changes in the electro-encephalogram observed during the progressive hypoglycaemia in hepatectomized animals.[7]

The evidence is that insulin is not necessary for the peripheral utilization of either fructose or mannose, but that mannose, possibly because of its greater affinity for the brain phosphorylating enzyme, hexokinase,[8] is much more effective in maintaining cerebral functions. It is to be hoped that in any further trials conducted along the lines suggested in your annotation mannose, as well as fructose, will be investigated.—I am, etc.,

London, Canada. R. J. ROSSITER.

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Congenital Hydrocephalus and Vitamin-A Deficiency

SIR,—Having worked for some years on vitamin-A deficiency,[1] I may perhaps comment on your annotation (*Journal*, April 3, p. 809). Your annotator rightly and cautiously underlines the importance of vitamin-A deficiency in the production of hydrocephalus in all 16 rabbits used in the Cambridge experiment.[2] However, most of the recent experimental work in this field has been carried out on rats. The offspring exhibited in decreasing frequency congenital defects of the eyes, diaphragm, urogenital system, aortic arch, and heart; administration of vitamin A to the deficient mothers at progressively earlier times during pregnancy resulted in a progressive decrease in the rate of malformations.[3] It was therefore surprising to learn[4] that an excessive intake of vitamin A in rats from the second to the sixteenth day of pregnancy causes gross developmental abnormality of the skull with an extrusion of the brain to the external surface of the head as well as more sporadic congenital abnormalities. As the quantity of vitamin A, not only its absence, in the antenatal diet seems to have an important influence on congenital defects, would it not be instructive to repeat the Cambridge experiments with an overdose of vitamin A?—I am, etc.,

London, W.1. Z. A. LEITNER.

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Undescended Testicles

SIR,—Dr. G. I. M. Swyer (*Journal*, April 3, p. 815) attacks Dr. N. S. Craig's letter (*Journal*, March 20, p. 706) as being reminiscent of a mediaeval schoolman because, in support of his opinion that hormone treatment of undescended testicles is futile, he follows the universal practice of scientists and quotes published work. What else is he to do? If Dr. Swyer follows up the references he has been given, he will find he is being referred not to opinion nor to authority, but to questions of verifiable fact, that is to say, of gross anatomy. The best way of stopping this method of treatment would be to get its enthusiasts (preferably accompanied by professors of anatomy) into the operating theatre, and there demonstrate to them the structure of the region they treat, and in particular the misconception on which their treatment depends. In my experience, however, this is impossible: and I would suggest that what is really reminiscent of mediaeval theologians is a refusal to examine the truth of statements which conflict with one's own opinions.

I see two or three cases every week which have been diagnosed as "undescended testicles." Of these some 80% are demonstrably normal, that is to say the testicles can, by those who know how to do it, be brought well into the scrotum. The less anatomical knowledge a practitioner has, the less skill in palpation, and the earlier he tackles these cases, the more "cryptorchids" he will find: there should also be a significant increase during spells of cold weather. Quite a number of these normal cases are sent along for operation because hormones have made no difference in their condition; when left alone the testicles take the normal adult position in their own good time. In my experience hormones are quite unreliable as a means of distinguishing the congenital deformities which need operation from the delayed descent which does not.

Originally hormones were written up as a cure for all varieties of cryptorchidism, and testicles were regularly reported as being brought out of the inguinal canal and the abdomen. In fact I have just received a commercial puff which advises that the testicle should not be brought out of the abdomen too rapidly, in order to give time for the processus vaginalis to close behind it in its flight. One early writer stated that so powerful was the action that he had known the testicle descend twenty minutes after the injection: in default of more exact information of what Dr. Swyer means by curing cases "there and then," I regard this as the record.

However, since I described the retractile testicle, and stated that hormone successes only occurred in this variety,[1] these claims are gradually being abandoned. Now hormones are used to distinguish between ectopic and retractile varieties, on the principle that if the treatment succeeds it is shown to have been unnecessary. I see a number of unilateral cases with one testicle well down in the scrotum which have had hormone treatment, apparently on the notion that in their case the natural substances have been confined to one side of the body. In two seen recently injections had gone on for three and four years respectively before hope and finance failed. As to the psychological aspect, worry about the absence of testes from the scrotum is unknown in the small children whose treatment is being advocated, whereas terror and distress are invariably caused by regularly recurring needle pricks. Worry about non-descent comes on late in development when nearly all cases are in need of surgery; it is curiously rare in any event.

Regarding the claim that in the congenital deformities the cord is lengthened by hormone treatment and facilitates operation, I have never found this effect myself, even after years of injections. I should be grateful for a reference to any exact work on this subject. I do know, however, of some interesting though alarming reports of the effect of hormones on the spermatogenic cells of the rats on whom the original work was founded.—I am, etc.,

London, W.1. DENIS BROWNE.

REFERENCE

1 *Proc. roy. Soc. Med.*, 1949, **42**, 643.